The Relationship between Blood Lead Levels and Periodontal Bone Loss in the United States, 1988–1994

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An association between bone disease and bone lead has been reported. Studies have suggested that lead stored in bone may adversely affect bone mineral metabolism and blood lead (PbB) levels. However, the relationship between PbB levels and bone loss attributed to periodontal disease has never been reported. In this study we examined the relationship between clinical parameters that characterize bone loss due to periodontal disease and PbB levels in the U.S. population. We used data from the Third National Health and Nutritional Examination Survey (NHANES III), 1988–1994, for the analyses. A total of 10,033 participants 20–69 years of age who completed a periodontal examination and had whole blood tested for lead were examined. Four types of periodontal disease measures were used to indicate oral bone loss: periodontal pocket depth, attachment loss extent, attachment loss severity, and the presence of dental furcations. We found that dental furcations were the best periodontal bone loss indicator for PbB levels ($p = 0.005$) in a multivariate linear regression model adjusting for sex, age, race/ethnicity, educational attainment, poverty status, smoking, and age of home. Furthermore, after additional modeling, we found a smoking and dental furcation interaction ($p = 0.034$). Subsequent stratified analyses indicated that current and past smoking is an effect modifier for dental furcations on PbB levels. These findings indicate that increased PbB levels may be associated with advanced periodontal bone loss, particularly among people with a history of smoking. *Key words:* **alveolar bone loss, blood lead, lead, NHANES, periodontal disease, smoking.** *Environ Health Perspect* **110:997–1002 (2002). [Online 28 August 2002]**
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Like calcium and fluorine, lead has an affinity for maturing bone. Calcified tissues, such as bone and teeth, are the principal sites for lead storage in adults and children, and bone represents more than 90% of the total body burden of lead in adults (Barry 1975; Schroeder and Tipton 1968). Once lead is incorporated into the crystalized architecture of bone, not only does it become a dormant structural component of the osseous matrix until osteoclastic activity can release it into the circulation (Klein and Wiren 1993; Rabinowitz 1991) but it also may be affected by bone resorption (Tsaih et al. 2001). Although the half-life of lead in the human skeleton is not well quantified, it could range into decades (Barry 1975; Rabinowitz et al. 1976; Steenhout 1982). Unlike the long residence time of lead in bone, the half-life of lead in blood is only 30 days (Rabinowitz 1991). Given the low mean bone turnover rates in adults (2–4% in persons ≥ 30 years of age), bone lead stores in adults represent years of accumulated exposure (Rabinowitz 1991). Consequently, skeletal sources of lead could be responsible for elevated blood lead (PbB) levels, even when lead exposure ended years ago (Rabinowitz 1998). In contrast to bone lead stores, lead in the circulation is not only an indicator of past exposure as lead is released from bone but of current environmental exposure as well (Hu et al. 1998).

The flux of lead into blood may be connected not only with normal bone turnover, but with periods of rapid bone metabolism as well. It has been suggested that PbB levels could be increased during pregnancy, lactation, mineral deficiencies from diet, and some disease conditions, such as hyperthyroidism and osteoarthritis (Gulson et al. 1995; Smith et al. 1996). It has also been reported that lead exposure may be associated with pediatric dental caries (Moss et al. 1999). Because it appears that accelerated bone turnover or mineral loss can contribute to increased lead in blood, it seems biologically plausible that bone loss from advanced periodontal disease would be associated with increased PbB levels.

Periodontal disease is characterized by periods of active destruction of the periodontium followed by periods of protracted inactivity. This waxing and waning nature of periodontal disease is insidious and often asymptomatic among many individuals. The chronic progression of the disease leads to irreversible alveolar bone loss that may advance to pocket depth formation and increase loss of clinical attachment of the tooth. The creation of a diseased periodontal pocket is the result of soft-tissue inflammation with inferiorly progressing alveolar bone loss (Figure 1). As the diseased pocket advances apically, tooth attachment is damaged and the supporting alveolar bone is destroyed, which increases the likelihood of tooth loss. Pocket depth may increase or decrease with advancing attachment loss in chronic periodontitis. For affected posterior teeth, significant attachment loss will lead to the destruction of alveolar bone between a tooth's roots, forming a dental furcation. Although there is no consistent pattern to the development of advanced periodontal bone loss, an individual must develop significant posterior attachment loss to acquire dental furcations. The most current epidemiologic findings from the United States indicate that 53% of adults 30–90 years of age have at least one dental site with ≥ 3 mm of loss of attachment, compared to nearly 64% who have ≥ 3 mm of pocket depth (Albandar et al. 1999). It is also well known that periodontal disease increases with age, that it is more prevalent in males, and that it is associated with smoking and some socioeconomic indicators.

Recent U.S. population findings indicate that older adults have higher PbB levels compared to younger adults, and current smokers are more likely to have higher PbB levels compared to nonsmokers (Pirkle et al. 1998). Moreover, cross-sectional results from the Normative Aging Study (a population-based study of men) indicate that bone lead concentrations are associated with age and smoking history and that increases in bone lead directly correspond to increases in PbB levels (Hu et al. 1996). Because age, smoking, and periodontal disease are significantly interrelated, studies investigating PbB levels should adjust for factors including advanced periodontal bone loss.

In this study, we examined the relationship between PbB levels and intra-oral bone loss associated with measurable dental clinical parameters indicative of periodontal disease. We hypothesized that moderate to severe periodontal bone loss may be a contributory source of lead in the circulation and that it is associated with increased PbB levels. Using a nationally representative sample, we examined the association of periodontal bone loss with increased PbB levels while controlling for confounding influences such as age and smoking.

Methods

Study population. We used data from 10,033 persons who participated in the Third National Health and Nutritional Examination Survey

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(NHANES III), 1988–1994. Conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC), NHANES III utilized a complex, highly stratified, multistage probability design capable of producing a nationally representative sample. Details of the sample design and methods used in obtaining informed consent from study participants have been described elsewhere (CDC 1994). NHANES III oversampled individuals who were ≤ 6 years of age, > 60 years of age, Mexican Americans, and non-Hispanic blacks. This was done to enhance the reliability of prevalence estimates for these groups in the noninstitutionalized civilian population of the United States.

A total of 17,030 participants ≥ 20 years of age who had completed the home interview component of NHANES III were examined. We excluded 3,358 individuals ≥ 70 years of age because of low participation rates (< 50%) in completing the sequence of interviewing, PbB testing, and having enough teeth to complete a periodontal examination. We then excluded 10 individuals who did not have PbB test results. From the remaining group, we excluded 1,721 persons who were edentulous or had < 6 natural teeth, and we excluded 1,903 additional individuals who did not have complete periodontal exam information. This yielded an analytical sample of 10,033 individuals for our study.

For this study, demographic data were obtained from a household interview questionnaire, and participants had a standardized oral health exam and venipuncture at a mobile examination center. The dental examinations were conducted by trained dentists who were periodically calibrated by the survey's expert dental examiner, and inter-rater reliability was considered to be good between the survey examiners and the reference examiner (Drury et al. 1996; Winn et al. 1999). PbB levels were measured by graphite furnace atomic absorption spectrophotometry (GFAAS) and are described elsewhere (Pirkle et al. 1998).

Covariate selection. For this analysis, we included known risk factors for PbB as well as periodontal disease. Race/ethnicity was categorized as Mexican American, non-Hispanic black, non-Hispanic white, and other. Individuals who were identified as "other" were included in the total population estimates but not in the regression analyses. Poverty status was dichotomized as either ≤ 130% of the federal poverty level or > 130% and was calculated by taking the quotient of total family income and the adjusted federal poverty income threshold. Educational attainment was dichotomized as either not completing high school or as having graduated from high school. Age and sex were also analyzed. Cigarette smoking status was categorized as either current smoker, former smoker, or never smoked. Persons who reported that they had smoked at least 100 cigarettes (approximately five packs) in their lifetime but no longer smoked cigarettes were classified as former smokers. Age of home, a known risk factor for elevated PbB, was categorized into three construction periods: before 1946, 1946–1973, and after 1973. The age of home categorization was established by the NCHS and publicly released in this format. Residential paint containing up to 50% lead was in widespread use through the 1940s; lead usage in residential paint declined thereafter and was banned in 1978 (CDC 1997).

Although we did not classify participants according to their periodontal disease status, we did identify certain clinical characteristics that could constitute disease when used with radiographs in a more appropriate diagnostic setting. These indicators of disease are periodontal attachment loss, pocket depth, and root furcations. Periodontal measurements for both attachment loss and pocket depth were made at the mid-facial and mesial facial interproximal sites on each permanent tooth in two randomly selected quadrants (i.e., one maxillary and one mandibular). The evaluation for the presence of dental root furcations was made only on the maxillary second bicuspid, first and second molars, and the mandibular first and second molars in the same randomly selected quadrants. Detailed information about the NHANES III oral health component protocol and measurement issues have been described elsewhere (CDC 1994; Drury et al. 1996).

We characterized attachment loss by two methods: an extent index and a mean bone loss score. For the disease extent index of attachment loss, the number of dental sites affected by clinical attachment loss was summed and divided by the number of dental sites evaluated. This ratio was categorized into four groups: 0–15% of the dentition affected, 16–30% of the dentition affected, 31–45% of the dentition affected, and ≥ 46% of the dentition affected. Clinical attachment loss, as an indicator of past periodontal disease, was defined as sites that had experienced a minium of 2 mm of measured loss. This criteria was established to reflect a previously published extent and severity attachment loss index (Carlos et al. 1986). For mean bone loss, attachment loss measured in millimeters at each dental site was summed and divided by the number of sites examined to produce a mean alveolar bone loss score. This score was categorized into three groups: < 1.5 mm of mean bone loss, 1.5–2.5 mm of mean bone loss, and > 2.5 mm of mean bone loss.

Periodontal pocket depth was expressed as a dichotomous variable indicating that at least one dentate site had a pocket depth of ≥ 5 mm. Periodontal probing depths in the range of 5 mm will generally classify an individual as a chronic periodontitis case with moderate destruction (Anonymous 2000). Both partial and complete furcal bony defect types were grouped to form a dichotomous variable that identified an individual as having either none or at least one dentate site affected by a dental furcation.

Data analysis. All statistical analyses were performed with SUDAAN, a software package specifically designed to accommodate complex sample surveys (Shah et al. 1996). We used sample weights to account for the unequal probability of selection and nonresponse of the study participants to produce estimates, regression coefficients, and related standard errors. We used the GEOMETRIC option within SUDAAN to calculate mean PbB levels. We assessed potential prevalence differences of PbB levels ≥ 10 μg/dL within the defined risk categories by calculating *t* statistics using a linear contrast procedure in SUDAAN.

We used linear regression models to estimate unadjusted and adjusted coefficients (coef.) and related SEs with statistical significance established at $p < 0.05$. Because PbB levels were not normally distributed, we used the $\log_{10}$ transformation of the PbB levels as the dependent variable. Except for age, all independent variables were modeled categorically as previously described. Age in years was analyzed as a continuous variable. For the multivariate linear regression analysis, we used nonautomatic stepwise regression modeling to assess the relationships between the covariates. Linear multivariate models were determined by covariate exclusion with criteria for inclusion set at $p < 0.05$. We modeled the periodontal indicators independently with the social/demographic and behavior covariates to examine relationships among the independent variables. To avoid potential multicollinearity

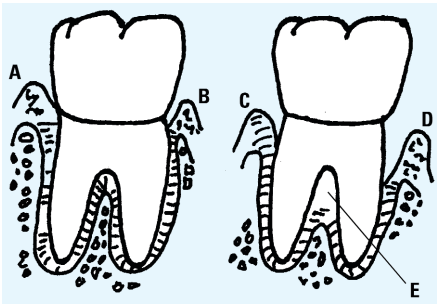

Figure 1. Schematic showing the progression of alveolar bone loss (not drawn to scale). A, Healthy periodontium with nondiseased pocket depth and no attachment loss; B, mild periodontitis with < 2 mm attachment loss and > 3 mm pocket depth; C, moderate periodontitis with > 2 mm attachment loss and > 4 mm pocket depth; D, advanced periodontal disease with > 4 mm attachment loss and > 6 mm pocket depth; E, dental furcation indicative of severe periodontal disease.

problems, the periodontal indicators were also individually assessed in separate multivariate models. Potential interactions were explored throughout the modeling process using multiple-level product terms.

Results

Data collected from 10,033 participants were used in this study, corresponding to approximately 73% of the total number of 20–69-year-old participants eligible for an exam. The geometric mean PbB level among the participants in this study was 2.5 µg/dL (Table 1). Geometric mean PbB levels were lower among 20–29-year-old adults compared to 60–69-year-old adults (2.0 µg/dL vs. 3.5 µg/dL). The PbB geometric mean was greater for men, those who did not graduate from high school, those in poverty, current cigarette smokers, residents of older homes, non-Hispanic blacks, and Mexican Americans. The PbB geometric mean was also greater for individuals with periodontal pockets ≥ 5 mm in depth (3.4 vs. 2.4 µg/dL) and with dental furcations (3.8 vs. 2.4 µg/dL) compared to those individuals without those periodontal conditions. The geometric mean PbB was incrementally greater as the extent of attachment loss and severity of alveolar bone loss increased.

The prevalence of individuals with PbB levels ≥ 10 µg/dL in this study group was 2.36% (Table 1). The remaining demographic and behavioral factors followed a similar pattern corresponding to the geometric mean results. Among persons with periodontal pockets ≥ 5 mm in depth, the prevalence of PbB levels ≥ 10 µg/dL was 4.46%. If an individual experienced a dental furcation, the prevalence of PbB levels ≥ 10 µg/dL was 7.20%. As the extent of attachment loss increased from < 15% to > 45%, elevated PbB level prevalence increased from 1.43% to 4.06%. Prevalence ranged from 1.88% to 9.58% as mean alveolar bone loss increased from < 1.5 mm to ≥ 2.5 mm, indicating a significant incremental increase ($p < 0.05$) that suggests a potential dose–response relationship between PbB levels and increasing alveolar bone loss.

Table 1. The weighted geometric mean (GM) PbB levels and the percentage of persons with PbB levels ≥ 10 µg/dL by selected characteristics for the total population.

Characteristic	Sample size	GM (SE)	Percent ≥ 10 µg/dL (SE)
Total	10,033	2.5 (0.08)	2.36 (0.32)
Sex			
Females[a]	5,255	1.9 (0.05)	0.66 (0.17)
Males	4,778	3.3 (0.12)	4.06 (0.59)*
Age group (years)			
20–29[a]	3,126	2.0 (0.07)	1.69 (0.42)
30–39	2,805	2.4 (0.09)	2.39 (0.59)
40–49	1,944	2.6 (0.08)	2.12 (0.35)
50–59	1,067	3.2 (0.14)	3.90 (0.91)*
60–69	1,091	3.5 (0.11)	3.27 (0.72)*
Race/ethnicity			
Mexican American	3,390	2.8 (0.08)	4.21 (0.49)*
Non-Hispanic black	2,859	2.8 (0.09)	4.01 (0.47)*
Non-Hispanic white[a]	3,352	2.4 (0.09)	2.09 (0.43)
Other[b]	432	—	—
Education			
Did not complete high school	3,357	3.1 (0.11)	5.20 (0.77)*
Completed high school[a]	6,619	2.4 (0.07)	1.73 (0.30)
Poverty (federal poverty line)			
≤ 130%	2,979	2.6 (0.10)	3.55 (0.59)*
> 130%[a]	5,989	2.4 (0.07)	2.02 (0.31)
Cigarette smoking status			
Current smoker	2,749	3.2 (0.10)	4.57 (0.72)*
Former smoker	2,009	2.6 (0.10)	2.13 (0.51)
Never smoked[a]	5,274	2.1 (0.06)	1.16 (0.28)
Year home was built			
Pre-1946	1,786	2.8 (0.13)	3.89 (0.70)*
1946–1973	4,381	2.5 (0.07)	1.47 (0.24)
Post-1973[a]	2,743	2.2 (0.10)	1.96 (0.54)
Periodontal pocket probing depth ≥ 5 mm			
Yes	1,072	3.4 (0.13)	4.46 (0.98)*
No[a]	8,961	2.4 (0.07)	2.20 (0.31)
Periodontal attachment loss (dentition affected)			
0–15%[a]	4,805	2.1 (0.06)	1.43 (0.32)
16–30%	1,283	2.5 (0.10)	1.41 (0.37)
31–45%	971	2.6 (0.12)	3.58 (1.0)
46–100%	2,759	3.3 (0.11)	4.06 (0.68)*
Mean total bone loss			
< 1.5 mm[a]	8,261	2.3 (0.07)	1.88 (0.29)
1.5–2.5 mm	1,256	3.5 (0.14)	3.60 (0.66)*
> 2.5 mm	516	4.5 (0.19)	9.58 (2.4)*
Presence of a dental furcation			
Yes	1,174	3.8 (0.17)	7.20 (1.4)*
No[a]	8,859	2.4 (0.07)	1.89 (0.28)

[a]Reference category. [b]Prevalence estimates and SEs are unreliable due to low sample size. *$p < 0.05$ when compared to the reference category.

Results from linear regression models are exhibited in Table 2. Simple (unadjusted) regression models showed that PbB levels in 20–69-year-old adults were significantly associated ($p < 0.0.5$) with males, increasing age, lower educational achievement, poverty, history of cigarette smoking, residing in an older home, the two minority race/ethnicity groups, and all four periodontal bone loss indicators. In a multivariate linear model, after stepwise regression modeling produced the most significant main effect covariates (Model 1), the only periodontal covariate significantly associated with PbB levels was the presence of a dental furcation ($p = 0.005$). Poverty was not significantly associated ($p > 0.05$) with higher PbB levels after adjusting for effects of periodontal bone loss. After additional modeling to identify potential multilevel interactions in a reduced multivariate model with significant risk indicators for higher PbB levels (Model 2), a significant interaction emerged between the effects of smoking status and the presence of a dental furcation ($p = 0.034$). The effects of this interaction were marginal among the remaining social/demographic covariates.

As a result of the smoking and dental furcation interaction, we performed a subanalysis stratified by smoking status. These results are present in Table 3. The presence of a dental furcation remained significantly associated with higher PbB levels for both current smokers ($p = 0.004$) and past smokers ($p = 0.015$). However, the presence of dental furcations was not associated with greater PbB levels among nonsmokers. The only other significant difference observed in the stratified analysis was that Mexican-American ethnicity was no longer associated with higher PbB levels for current and former smokers.

Discussion

In this analysis of more than 10,000 persons representative of the U.S. population 20–69 years of age, we found a strong association between advanced periodontal bone loss and higher PbB levels. The finding that moderate to severe periodontal bone loss defined by the presence of a dental furcation is associated with higher PbB levels and that this association was not homogenous across the smoking strata is an important consideration for identifying higher PbB levels in adults. Moreover,

these findings suggest that preventing the development of advanced periodontal disease and promoting smoking cessation may beneficially affect PbB levels.

The presence of an interaction between dental furcations and smoking status in the regression modeling is a significant finding. Although the effects of smoking on periodontal health have been well reported (Tomar and Asma 2000), the systemic consequences of smoking and advanced periodontal disease have not been described beyond the chronic inflammatory effects that have been suggested as potential contributors of coronary heart disease, atherosclerosis, and cerebrovascular disease (Arbes et al. 1999; Beck et al. 1996; Hujoel et al. 2000; Kiechl et al. 2001; Wu et al. 2000). Furthermore, most studies have reported only main effect terms, suggesting that a potential smoking and periodontal disease interaction is absent when the outcome under study is a chronic inflammatory disease. Our results suggest that smoking and advanced periodontal disease interact qualitatively on chronic conditions, such as PbB levels, which potentially may affect systemic health.

Because the presence of dental furcations is not consistent across all three smoking categories, our findings indicate that smoking is not only a confounder in the relationship between periodontal bone loss and higher PbB levels but it is a significant effect modifier for this relationship. These findings also indicate that the effects of smoking status on PbB levels are not consistent by race/ethnicity as well. Unlike the presence of dental furcations, Mexican-American ethnicity is not associated with PbB levels among current and former smokers, but it is associated with PbB levels among nonsmokers. These findings support the notion that nonsmoking or smoking cessation before the occurrence of moderate to severe bone loss may have an important impact on the potential risk for higher PbB levels.

Dental furcations are an indicator not only of the severity of bone loss but often of the magnitude of posterior dental attachment loss. The length of time required for furcation development may explain why dental furcations are a stronger indicator for increasing PbB levels than are attachment loss measures. It has been reported that significant attachment loss foreruns radiographic bone loss by 6–8 months (Goodson et al. 1984). Thus, clinical attachment loss measures may also detect potential pre–bone-loss activity, whereas dental furcation assessments measure actual clinical bone loss.

Another measure of periodontal health, periodontal pocket depth, was not a significant factor for higher PbB levels. Although pocket depths measuring ≥ 5 mm demonstrated a significant association with PbB levels in the univariate analysis, this relationship disappeared when more precise measures of alveolar bone loss were incorporated into multivariate analyses. Because pocket depth measurements are not only influenced by the degree of bone destruction present but also by the magnitude of the surrounding soft-tissue inflammation, these results are biologically meaningful. Thus, only the portion of bone loss attributable to the pocket depth measurement would contribute to increased PbB levels. Therefore, compared to attachment loss, the same magnitude of pocket depth would have less influence on circulatory blood lead.

In a linear model that included all of the main effect terms for social/demographic, behavior, and periodontal bone loss indicators, the only periodontal indicator to remain significant in a parsimonious model was the presence of a dental furcation. This finding may have been influenced by the effects of multicollinearity among the periodontal bone loss variables. Results from a correlation analysis (data not shown) indicated that the Spearman's rank correlation coefficient ranged from 0.35 to 0.57 between the periodontal indicators. Results from a bivariate analysis showed that 76% of individuals with dental furcations also had attachment loss > 45%. In this context, individuals with a furcation have the most advanced or the more severe forms of dental bone loss.

Although the effects of increased PbB in children, as low as 10 µg/dL, have been widely documented, particularly for cognitive disabilities and learning disorders, less has been reported on the effects of PbB levels ≤ 10 µg/dL in adult populations. It has been reported that lead impedes the biosynthesis of heme and can increase erythrocyte fatality at low PbB levels. Hernberg et al. (1971) reported that at PbB levels <10 µg/dL, δ-amino levulinic acid dehydratase (ALAD) is partially inhibited by lead, and at 30 µg/dL,

Table 2. Linear regression results [coefficients (β), SEs, and *p*-values] using log PbB levels for the total population.[a]

	Unadjusted		Model 1		Model 2	
Characteristic	β (SE)	*p*-Value	β (SE)	*p*-Value	β (SE)	*p*-Value
Sex						
Male	0.59 (0.02)	0.000	0.52 (0.02)	0.000	0.52 (0.02)	0.000
Female	Reference					
Age (years)[b]	0.01 (0.00)	0.000	0.02 (0.00)	0.000	0.02 (0.00)	0.000
Race/ethnicity						
Mexican American	0.14 (0.05)	0.004	0.16 (0.05)	0.002	0.16 (0.05)	0.003
Non-Hispanic black	0.14 (0.04)	0.001	0.20 (0.04)	0.000	0.20 (0.04)	0.000
Non-Hispanic white	Reference					
Education						
Did not complete high school	0.28 (0.03)	0.000	0.14 (0.03)	0.001	0.14 (0.03)	0.000
Completed high school	Reference					
Poverty (federal poverty line)						
≤ 130%	0.07 (0.03)	0.003	—		—	
> 130%	Reference					
Cigarette smoking status						
Current smoker	0.45 (0.02)	0.000	0.38 (0.02)	0.000	NR	
Former smoker	0.25 (0.03)	0.000	0.08 (0.03)	0.011	NR	
Never smoked	Reference					
Year home was built						
Pre-1946	0.24 (0.05)	0.000	0.21 (0.05)	0.001	0.21 (0.05)	0.000
1946–1973	0.09 (0.04)	0.031	0.03 (0.04)	0.362	0.03 (0.04)	0.367
Post-1973	Reference					
Periodontal pocket probing depth ≥ 5 mm						
Yes	0.35 (0.03)	0.000	—		—	
No	Reference					
Periodontal attachment loss (dentition affected)						
46–100%	0.47 (0.03)	0.000	—		—	
31–45%	0.23 (0.04)	0.000	—		—	
16–30%	0.17 (0.04)	0.000	—		—	
0–15%	Reference					
Mean total bone loss						
> 2.5 mm	0.66 (0.04)	0.000	—		—	
1.5–2.5 mm	0.41 (0.03)	0.000	—		—	
< 1.5 mm	Reference					
Any furcation present						
Yes	0.48 (0.04)	0.000	0.13 (0.05)	0.005	NR	
No	Reference					
Interaction between furcation and smoking	—		—		0.10 (0.05)	0.034

NR, not reported. A dash (—) indicates that the covariate was not included in the model.
[a]Simple (unadjusted) and multivariate (adjusted) linear regression models were used. Model 1 covariates include sex, age, race/ethnicity, education, smoking, age of home (when built), and dental furcation; Model 2 covariates include sex, age, race/ethnicity, education, smoking, age of home(when built), dental furcation, and the interaction term for smoking and dental furcation. [b]Age was used as a continuous variable.

ALAD inhibition is 50% complete. Suppressive activity at this enzymatic level reduces monopyrrole porphobilinogen, the primary building block for all hemes and vitamin B_{12} derivatives. Furthermore, Smith et al. (1996) reported that the effects of lead toxicity may impede osteoblastic function and that alkaline phosphatase activity is diminished in a time- and dose-dependent way. Lead decreases osteoid formation and increases osteoclastic activity in rabbits (Hass et al. 1964), decreases osteoblasts in dogs (Anderson and Danylchuk 1977), and decreases bone density in rats, which suggests that lead may be a risk factor for osteopenia (Gruber et al. 1997). Silbergeld (1991) postulated that endogenous lead released as a result of accelerated bone metabolism during disease or pregnancy and lactation may be an important risk factor in the assessment of potential lead toxicity for some individuals. It was also suggested by Lippman (1990) that relatively small increases of PbB levels within the range of 5–30 μg/dL could have significant effects on elevating blood pressure in adults.

The mean PbB level among adults in the United States in 1991–1994 ranged from 2.1 μg/dL in persons 20–49 years of age to 3.4 μg/dL in those ≥ 70 years of age (Pirkle et al. 1998). In a study using endogenous stable lead isotopes in subjects exposed to low-level, exogenous sources of lead (1–6 μg/dL PbB levels), Smith et al. (1996) estimated that 40–70% of lead in blood could be attributed to skeletal lead release. Consequently, a significant fraction of very low lead levels in blood is representative of normal bone homeostasis. With the possibility that normal bone turnover contributes at least half of the circulating elemental lead, a pathogenic increase in bone turnover should increase PbB levels as well. In a recent study, Adachi et al. (1998). concluded that accelerated bone turnover due to disease could be associated with lead resorption and absorption in trabecular bone. However, the biological processes that underlie this association are unclear.

In our analyses, we used demographic characteristics that are well-known prognostic indicators for increased PbB levels. The poverty covariate was initially categorized as either ≤ 130%, > 130 to < 200%, or ≥ 200% of the federal poverty level. Because there were no observed differences in estimates and regression results between individuals in the two higher levels, the > 130 to < 200% and the ≥ 200% poverty groups were collapsed into one group to create a dichotomous poverty categorical variable. Education was originally categorized as either having not completed high school, having graduated from high school, or having attended college. For reasons similar to poverty level, the education covariate was redefined as either having not completed high school or having graduated from high school. Other potentially important risk factors evaluated, but removed from the final analyses due to lack of significance, were metropolitan status and census region. Occupation was not included as a covariate because NHANES III did not sufficiently detail occupational information to appropriately classify potential worker-related exposure to occupational lead. Furthermore, it is estimated that < 1% of the employed adults in this data set would have had occupational exposure to lead; thus, influences originating from occupational status should not significantly bias our findings.

A limitation of our study is the use of a cross-sectional design to examine indicators for increased PbB levels, which prevents a definitive exploration of causality. However, we believe that the most likely direction for the observed association indicates that alveolar bone loss promotes increased PbB levels. Because periodontal disease is a progressively chronic disorder, and a portion of PbB levels may be related to prolonged release from the skeleton, the design of this study does not effectively address temporal relationships. Moreover, misclassification of exposure may have obscured our findings because of our inability to separate PbB levels from endogenous and exogenous sources. However, a significant cohort effect based on exogenous exposure was not anticipated because our study was likely limited to adults who experienced elevated environmental lead levels as children before the beginning of governmental regulation of lead sources in the United States in the mid-1970s. Finally, it has been reported that one-half of mouth examinations underestimate periodontal disease sites, particularly the more severe conditions (Ainamo and Ainamo 1985; Hunt and Fann 1991; Kingman et al. 1988). Although a limitation of our study was that the periodontal indicators were derived from a partial mouth examination, the direction of the bias produced from underreporting disease may have underestimated the magnitude of the association between periodontal bone loss and PbB. A strength of our study is its use of a large, nationally representative sample of adults to explore and control for multiple risk factors.

This is the first epidemiologic study to demonstrate a positive association between increased PbB levels and clinical parameters characteristic of bone loss attributed to advanced periodontal disease. Although prior experimental studies have described a relationship between PbB levels and bone metabolism either as a result of disease or normal physiologic turnover, our study is the first to explore intra-oral bone loss as a contributory factor for higher PbB levels. Although our study design prevents exploration of causality, our study promotes the notion that a relationship may exist between higher PbB levels and bone loss from periodontal disease, particularly in the presence of smoking. Our findings also suggest that smoking may act synergistically with diseased bone to increase PbB levels. Our analyses suggests that dental furcations have a similar magnitude of effect on PbB levels compared to known sociodemographic determinants such as educational attainment and race/ethnicity. Consequently, severe periodontal bone loss may have important clinical relevance. Because smoking and periodontitis are mediated by behavioral influences, effective health promotion and intervention activities aimed at reducing smoking and improving oral health may affect PbB levels. Given the

Table 3. Linear regression results [coefficients (β), SEs, and *p*-values] stratified by smoking status using log PbB levels for the total population and controlling for all other independent risk factors.[a]

	Current smoker (n = 2,317)[b]		Former smoker (n = 1,771)[b]		Nonsmoker (n = 4,401)[b]	
Characteristic	β (SE)	*p*-Value	β (SE)	*p*-Value	β (SE)	*p*-Value
Sex						
Male	0.56 (0.04)	0.000	0.40 (0.05)	0.000	0.55 (0.02)	0.000
Female	Reference					
Age (years)[c]	0.02 (0.00)	0.000	0.02 (0.00)	0.000	0.02 (0.00)	0.000
Race/ethnicity						
Mexican American	0.09 (0.06)	0.119	0.15 (0.08)	0.068	0.19 (0.05)	0.001
Non-Hispanic black	0.25 (0.05)	0.000	0.24 (0.06)	0.000	0.16 (0.04)	0.001
Non-Hispanic white	Reference					
Education						
Did not complete high school	0.14 (0.04)	0.002	0.15 (0.07)	0.037	0.14 (0.04)	0.002
Completed high school	Reference					
Year home was built						
Pre-1946	0.15 (0.07)	0.023	0.17 (0.06)	0.009	0.25 (0.07)	0.001
1946–1973	–0.01 (0.05)	0.781	–0.00 (0.04)	0.975	0.08 (0.04)	0.073
Post-1973	Reference					
Any furcation present						
Yes	0.21 (0.07)	0.004	0.17 (0.07)	0.015	–0.02 (0.07)	0.747
No	Reference					

[a]Multivariate linear regression models were used. [b]Total observations in the analysis. [c]Age was used as a continuous variable.

results of our findings, not only is additional research needed to further examine and describe the relationship between periodontal bone loss and higher PbB levels, but also to evaluate the health effects of increased PbB levels in adults.

References

Adachi JD, Arlen D, Webber CE, Chettle DR, Beaumont LF, Gordon CL. 1998. Is there any association between the presence of bone disease and cumulative exposure to lead? Calcif Tissue Int 63:429–432.

Albandar JM, Brunelle JA, Kingman A. 1999. Destructive periodontal disease in adults 30 years of age and older in the United States, 1988-94. J Periodontology 70(1):13–29.

Ainamo J, Ainamo A. 1985. Partial indices as indicators of the severity and prevalence of periodontal disease. Int Dent J 35:322–326.

Anderson C, Danylchuk KD. 1977. The effect of chronic low level lead intoxication on the Haversian remodeling system in dogs. Lab Invest 37:466–469.

Anonymous. 2000. Parameter on chronic periodontitis with slight to moderate loss of periodontal support. American Academy of Peridontology. J Periodontol 71(5 suppl):853–855.

Arbes SJ, Slade GD, Beck JD. 1999. Association between extent of periodontal attachment loss and self-reported history of heart attack: an analysis of NHANES III data. J Dent Res 78(12):1777–1782.

Barry P. 1975. A comparison of concentrations of lead in human tissues. B J Ind Med 32:119–139.

Beck J, Garcia R, Heiss G, Vokonas PS, Offenbacher S. 1996. Periodontal disease and cardiovascular disease. J Periodontol 67:1123–1137.

Carlos JP, Wolfe MD, Kingman A. 1986. The extent and severity index: a simple method for use in epidemiologic studies of periodontal disease. J Clin Periodontol 13:500–505.

CDC. 1994. Plan and operation of the Third National Health and Nutritional Examination Survey, 1988–94. Series 1: programs and collection procedures. Vital Health Stat 1(32):1–407.

CDC. 1997. Update: blood lead levels—United States, 1991–1994. MMWR 46(7):141–146.

Drury TF, Winn DM, Snowden CB, Kingman A, Kleinman DV, Lewis B. 1996. An overview of the oral health component of the 1988–91 National Health and Nutritional Examination Survey (NHANES III, phase 1). J Dent Res 75(Spec No):620–630.

Goodson JM, Haffajee AD, Socransky SS. 1984. The relationship between attachment level loss and alveolar bone loss. J Clin Periodontol 11:48–59.

Gruber HE, Gonick HC, Khalil-Manesh F, Sanchez TV, Motsinger S, Meyer M, et al. 1997. Osteopenia induced by long-term, low- and high-level exposure of adult rat to lead. Miner Electrolyte Metab 23(2):65–73.

Gulson BL, Mahaffey KR, Mizon KJ, Korsch MJ, Cameron MA, Vimpani G. 1995. Contribution of tissue lead to blood lead in adult female subjects based on stable lead isotope methods. J Lab Clin Med 125(6):703–712.

Hass GM, Brown D, Eisenstein R, Hemmens A. 1964. Relations between lead poisoning in rabbit and man. Am J Pathol 45:691–727.

Hernberg S, Nikkanen J, Mellin G, Lillius H. 1971. δ-Aminolevulinic acid dehydrase activity in red blood cells. Arch Environ Health 23:440–445.

Hu H, Payton M, Korrick S, Aro A, Sparrow D, Weiss ST, Rotnitzky A. 1996. Determinants of bone and blood lead levels among community-exposed middle-aged to elderly men: the Normative Aging Study. Am J Epidemiol 144(8):749–759.

Hu H, Rabinowitz MB, Smith D. 1998. Bone lead as a biological marker in epidemiologic studies of chronic toxicity: conceptual paradigms. Environ Health Perspect 106:1–7.

Hujoel PP, Drangsholt M, Spiekerman C, DeRouen TA. 2000. Periodontal disease and coronary heart disease risk. JAMA 284:1406–1410.

Hunt RJ, Fann SJ. 1991. Effect of examining half the teeth in a partial periodontal recording of older adults. J Dent Res 70:1380–1385.

Kiechl S, Egger G, Mayr M, Wiedermann CJ, Bonora E, Oberhollenzer F, et al. 2001. Chronic infections and the risk of carotid atherosclerosis. Circulation 103:1064–1070.

Kingman A, Morrison E, Loe H, Smith J. 1988. Systematic errors in estimating prevalence and severity of periodontal disease. J Periodontol 59:707–713.

Klein RF, Wiren KM. 1993. Regulation of osteoblastic gene expression by lead. Endocrinology 132(6):2531–2537.

Lippman M. 1990. Lead and human health: background and recent findings. Environ Res 51:1–24.

Moss ME, Lanphear BP, Auinger P. 1999. Association of dental caries and blood lead levels. JAMA 281:2294–2298.

Pirkle JL, Kaufmann RB, Brody DJ, Hickman T, Gunter EW, Paschal DC. 1998. Exposure of the U.S. population to lead, 1991–1994. Environ Health Perspect 106:745–750.

Rabinowitz MB, Wetherill GW, Kopple JD. 1976. Kinetic analysis of lead metabolism in healthy humans. J Clin Investig 58:260–270.

Rabinowitz MB. 1991. Toxicokinetics of bone lead. Environ Health Perspect 91:33–37.

Rabinowitz MB. 1998. Historical perspective on lead biokinetic models. Environ Health Perspect 106(suppl 6):1461–1465.

Schroeder HA, Tipton IH. 1968. The human body burden of lead. Arch Environ Health 17:965–978.

Shah B, Barnwell B, Bieler G. 1996. SUDAAN User's Manual, Release 7.0. Research Triangle Park, NC:Research Triangle Institute.

Silbergeld EK. 1991. Lead in bone: implications for toxicology during pregnancy and lactation. Environ Health Perspect 91:63–70.

Smith DR, Osterloh JD, Flegal AR. 1996. Use of endogenous, stable lead isotopes to determine release of lead from the skeleton. Environ Health Perspect 104:60–66.

Steenhout A. 1982. Kinetics of lead storage in teeth and bones: an epidemiologic approach. Archiv Environ Health 37(4):224–231.

Tomar S, Asma S. 2000. Smoking-attributable periodontitis in the United States: Findings from NHANES III. National Health and Nutrition Examination Survey. J Periodontol 71:743–751.

Tsaih S, Korrick S, Schwartz J, Lee M-LT, Amarasiriwardena C, Aro A, et al. 2001. Influence of bone resorption on the mobilization of lead from bone among middle-aged and elderly men: the Normative Aging Study. Environ Health Perspect 109:995–999.

Winn DM, Johnson CL, Kingman A. 1999. Periodontal disease estimates in NHANES III: clinical measurement and complex sample design issues. J Public Health Dent 59(2):73–78.

Wu T, Trevisan M, Genco RJ, Dorn JP, Falkner KL, Sempos CT. 2000. Periodontal disease and risk of cerebrovascular disease. Arch Intern Med 160:2749–2755.